Short Communication

Interference of Maternal Derived Immunity Against Vaccination with Baculovirus H5 and ND Inactivated Vaccine

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Abstract | Newcastle disease virus (NDV) and avian influenza viruses (AIVs) $H5N_1$ are endemic in Egypt and extensive vaccinations are being applied for chicken flocks, which have maternal derived antibodies (MDA) for these viruses. To understand the interference of maternal derived immunity impact of maternal derived immunity interference in vaccination regimen in poultry, a total of one hundred day old commercial broiler chicks were vaccinated with LaSota. A group of chicks (n=40) were immunized using baculovirus (H5 and ND) inactivated vaccine *via* subcutaneous route. Birds (n=20) were then either challenged with 10^6 EID_{50} using Egyptian avian influenza H5N1 and Newcastle disease genotype VII. Comparative blood profiling in vaccinated and challenged, non-vaccinated and non-challenged and non-vaccinated and challenged indicated that MDA for H5N1 gradually decreased from 5.1 to 0.4 log^2 and disappeared with in a month. While MDA for NDV remained 2.1 log^2 until 28th day of age, the Geometric mean titers (GMT) for H5 were increased from the 7th day of age using both antigens (RE-5 antigen) and (S75/Egy/2015 antigen). Generally, GMT post-challenge was increased as the chicks overcome the infections. In conclusion, our results indicate that vaccination at 5th day old with baculovirus H5+ND inactivated vaccine can interfere with MDA of H5 vaccine and has negative impact on H5 vaccine titer. However, NDV titer remained unaffected under same experimental conditions. These findings highlight the need of country or region specific optimization of vaccination schedules for viral infections to obtain optimized vaccine-induced protections.

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Introduction

Broiler farms in Egypt are exposed to multiple infections, most of them become enzootic and cause economic losses. Infections such as Newcastle disease virus (NDV) and avian influenza viruses are the main restriction to backyard poultry rearing in the developing countries. In non-vaccinated flocks, the mortality rate may reach up to 100% (Spradbrow, 1992). NDV and influenza viruses including $H5N_1$ are endemic in the Egyptian poultry sector and excessive use of vaccines is employed mass vaccination is being applied to control the infections. However, maternal derived antibodies (MDA) can provide protection but can also interfere with the vaccine-induced antibodies.

Velogenic ND and avian influenza viruses have become the most disaster in the poultry industry all over

the world (Swayne, 2003; Tadelle, 2004). In Egypt the first case of influenza appeared in 2006 (Aly, 2006) and since then the disease remain endemic and devastating for the industry. Vaccination could be a helpful tool in controlling influenza outbreaks followed by good monitoring and biosecurity tools applications, but there were many factors affecting on vaccine efficacy and vaccination strategies such as maternally derived antibodies, which can guard young chickens against viral diseases (Otaki et al., 1992; Mondal and Naqi, 2001; Nemeth and Bowen, 2007). On the other hand, maternal antibodies can also hinder vaccination due to rising clearance of vaccine antigens, which may prevent maximum exposure to the immune system (Naqi et al., 1983; Van Eck et al., 1991). For the vaccination of chicks against viral poultry diseases such as ND, live vaccines are commonly used. Depending on the antibody titers and the virulence of vaccine viruses, it is important to optimize the suitable time of vaccination (Solano et al., 1986). Previous studies reported that decreasing the efficacy of live vaccines in chickens with maternal immunity cannot be generalized to influenza vaccination, as the vaccines contain inactivated virus. Inactivated poultry vaccines are commonly used as a booster before the laying period to prompt efficient and homogenous antibody titers. It is important to compare the benefits of maternal immunity (i.e. guard against H5N1) with the negative impact maternal immunity may occur on vaccine efficacy. Due to these shortcomings in poultry sectors, risk time can be estimated in which chicken flocks are susceptible for HPAI H5N1 infection and cannot yet be vaccinated. If there is such a period, alternative vaccination strategies must be considered, as good biosecurity measures to overcome this period without any economic losses.

Material and Methods

Vaccines

Volvac® baculovirus-expressed inactivated H5-NDV vaccine (Lot no.1408024 A.) Avian Influenza (Baculovirus Expressed H5) + Newcastle disease Inactivated vaccine was used. The vaccine preparation contained 256 HA units of the H5 antigen (AI) and 128 HA units of the Newcastle disease virus antigen per dose (0.5ml). The H5 antigen is insect-cell-expressed H5 (recH5). Insect cells were infected with a recombinant baculovirus encoding the hemagglutinin (HA) protein of an HPAI A/duck/China/E319-2/2003 (H5N1) belonging to clade 2.3.2 and fusion (F) protein of Lasota strain (genotype II).

Animal experiments

One hundred commercial chicks (Hubbard) were divided into 5 groups (n=20 in each group) that were vaccinated with LaSota vaccine using spray on one-day of age as routine vaccination regime in a commercial chicks company in the hatchery. Following groups were used in this study:

Group 1: Chicks not vaccinated and not challenged (negative control)
Group 2: Chicks not vaccinated and challenged with H5N1 virus (H5 positive control)
Group 3: Chicks not vaccinated and challenged by vNDV genotype VII (NDV positive control).
Groups 4: commercial chicks were vaccinated with baculovirus-expressed H5+ND inactivated vaccine 0.5 ml per dose s/c. injection at 5th day old and were challenged by H5N1 virus then vNDV genotype VII with 3 days intervals.
Groups 5: commercial chicks were vaccinated with baculovirus-expressed H5+ND inactivated vaccine 0.5 ml per dose s/c. injection at 5th day old challenged by H5N1 virus only at 21 days post vaccination.

Challenge viruses

Purified Egyptian virus A/chicken/Egypt/1575s/2015 (H5N1) HPAI H5N1 clade 2.2.1.2/2015 (S75/EGY/2015) and NDV-B7-RLQP-CH-EG-12 as vNDV genotype VII NDV were used in the challenge experiments. Birds of each group were challenged at 21st days post-vaccination with 10^6EID_{50} in 100 ul of allantoic fluid dose per bird by intra-nasal route. The challenge viruses' titers were determined by back-titration.

Sampling and Serology

At 1st day of age serum samples were collected from 10 birds then collection each week from all groups until the day of challenge and 1st and 2nd week post challenge.

HA assay was performed according to the recommendation of the OIE (OIE, 2009). HI assay was performed for individual serum samples collected at 11st, 7th, 14th and 21st days pre-challenge and 7th and 14th days post-challenge using 4 HAU of H5N1&NDV antigens. Reference antigens and antisera for NDV

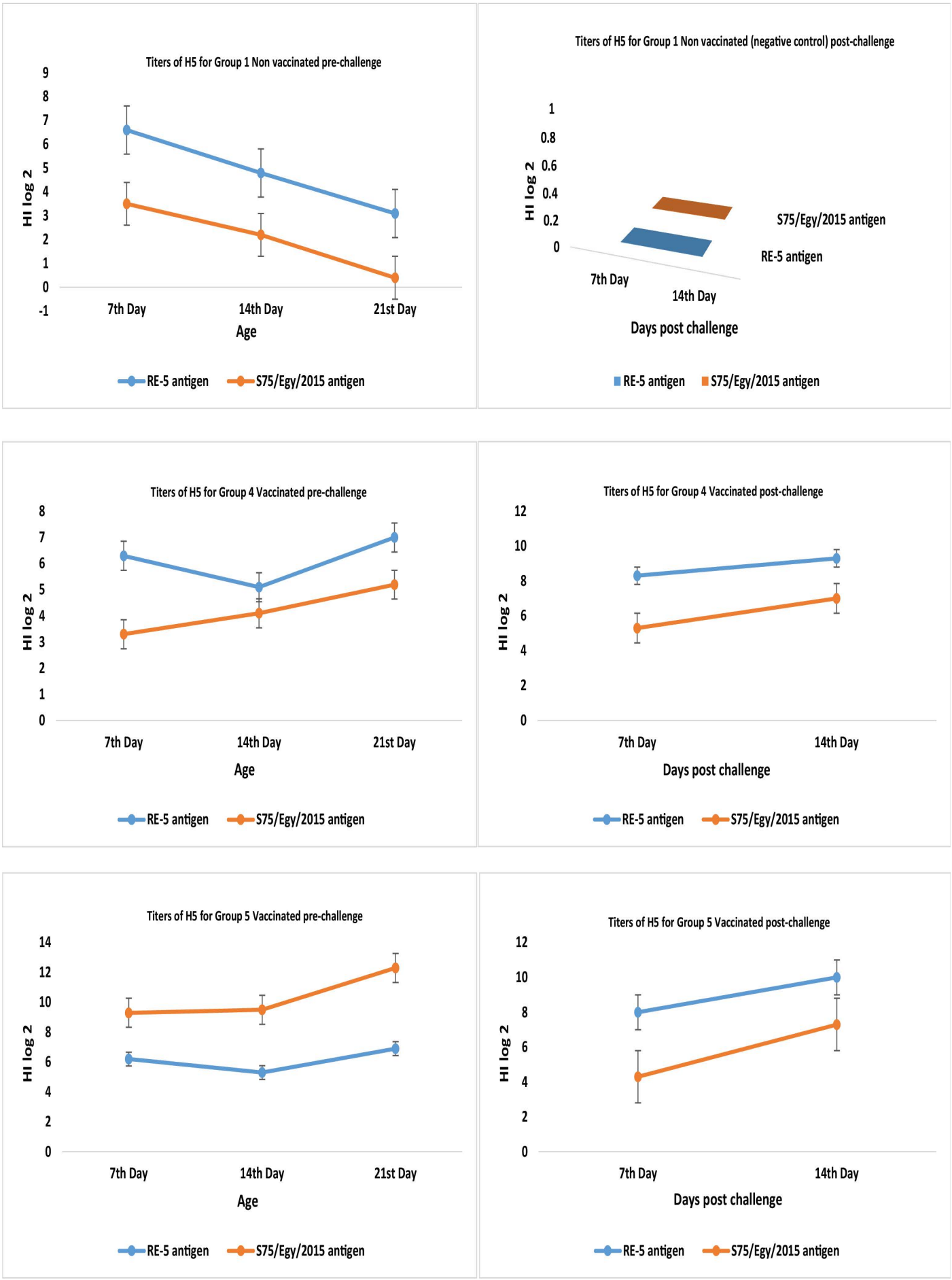

Figure 1: *HI titers of H5 by both RE-5 and S75 antigens pre- and post- challenge.*

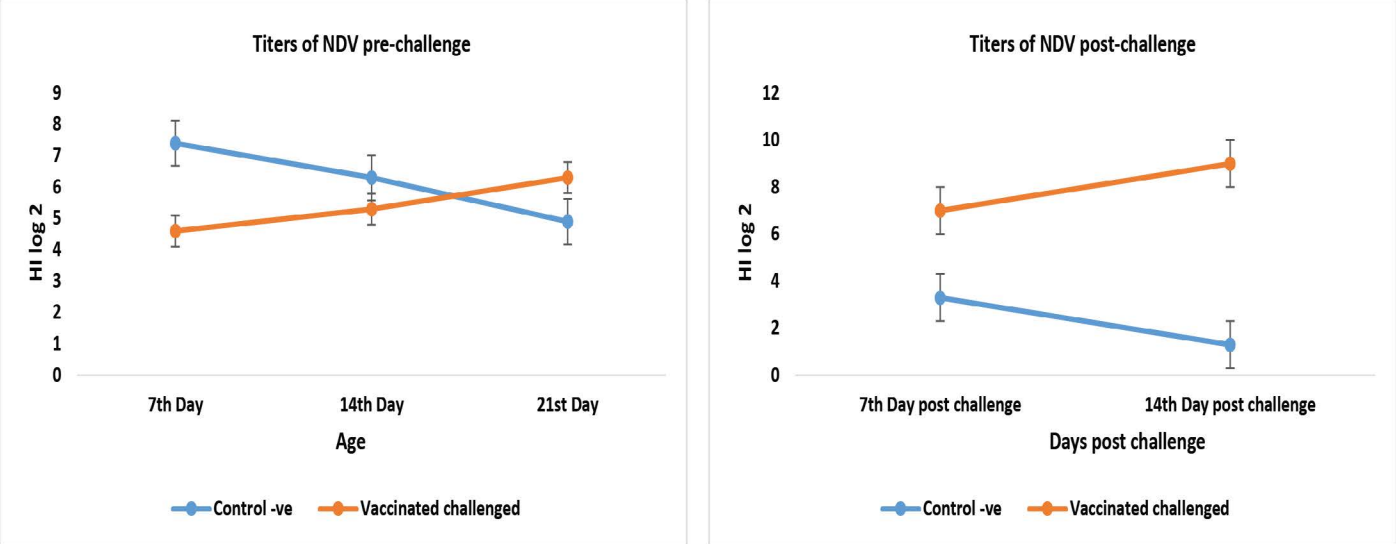

Figure 2: *HI titers of NDV pre- and post- challenge.*

(LaSota) and AI used in HA and HI assays were supplied from local agency of GD Lab., (Holland). The H5 antigen (RE-5) was kindly provided from Zheng Zhou Biopharmaceutical factory (Batch no: 150303 exp. Date: 05/3/2016 Mfd:6/3/2015 QYH).

Results and Discussion

Maternally derived antibodies guard young chicks against viral diseases (Otaki et al., 1992; Mondal and Naqi, 2001; Nemeth and Bowen, 2007). On the other hands, after routine vaccination of the breeders, high levels of MDAs are transferred to the progeny. MDAs provide some protection during the early life of chicks when the immune system is not yet fully developed, but they also interfere with successful vaccination of these young chicks because of their ability to neutralize, at least partially, the vaccine's virus and increase the clearance of the vaccine antigens, thereby preventing the optimal exposure to the immune system (Abdelwhab et al., 2012; De Vriese et al., 2010; Maas et al., 2011; Poetri et al., 2011; Akhtar et al 2017). In this study, the GMT for H5 decreased by time in non-vaccinated groups till almost disappeared (0.4 $\log^2$) at the 3rd week of age. It is thus likely that MDA in chickens are high after hatching, and reduced to zero within 3 or 4 weeks. The GMT for H5 in vaccinated groups were 7 $\log^2$ with RE-5 antigen and 5.2 $\log^2$ with S75 antigen at the 3rd week of age (Figure 1) while the GMT post-challenge was increased from 8.3 $\log^2$ - 9.3 $\log^2$ and 5.3 $\log^2$-7 $\log^2$ by RE-5 and S75 antigens respectively in group 4 (Figure 1). In case of single infection with H5 (group 5) the GMT increased from 8 $\log^2$-10 $\log^2$ by RE-5antigen and from 4.3 $\log^2$-7.3 $\log^2$ with S75 antigen at 14th day post-challenge (Figure 1). On the other hand, the percentage of protection was 70%-80% in group 4 and 5 post-challenge, respectively (data not shown). Similar to observations made by Maas et al. 2011, the chickens should have HI-antibody titers higher than 2^4 to be protected against clinical disease and reduce the virus shedding upon infection.

From the field experience, vaccinated chickens with quantifiable HI antibody titers are usually guarded against clinical disease post-infection with HPAIV, as has been detected for vaccination against H7N7 (Maas et al., 2009). However, morbidity and mortality can be seen in some chickens with HI antibody titers of below 2^3 log2 after challenge with a high dose of HPAIV $H5N_1$. So, at least 2^5 log2 antibody titer is being required to have efficient clinical protection in chickens with maternal immunity (Maas et al., 2011). Breeder chickens are mainly vaccinated against viral diseases by live vaccines at a young age, followed by boaster vaccination with inactivated vaccines before production. In particular, this is able to inhibit diseases such as Newcastle disease and Gumboro disease (infectious bursal disease). In case of AI, only the inactivated vaccine is permissible. Inactivated vaccines could stimulate a systemic antibody response, while live vaccines stimulate a broader immune response through infection of targeted cells and stimulation of the immune system similar to natural infection (Figure 2) (Maas et al., 2011).

In conclusion, it is recommended to delay the vaccination with baculovirus-expressed H5+ND inacti-

vated vaccine in broilers to 10th-14th day of age as the MDA will be in the decline phase to avoid its negative impact on the vaccine efficacy.

Authors Contirbution

Mahmoud Said, Mohammed A. Rohaim and Hussein A. Hussein drafted and revised the manuscript. Mahmoud Said, Abd El Satar Arafa attended to the case and performed animal experiments and follow-up. All authors contributed to the writing of the manuscript and approved it for submission.

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